

WHAT IS CLAIMED IS:

1. A method of diagnosing Alzheimer's disease comprising the step of genotyping the Alpha-2-Macroglobulin locus of an individual.
2. The method of claim 1, wherein said genotyping step comprises the steps of:
 - (a) isolating nucleic acid from an individual;
 - (b) amplifying the nucleic acid to generate an *A2M* fragment;and
 - (c) analyzing the fragment thereby correlating *A2M* genotype with the occurrence of Alzheimer's disease.
3. The method of claim 2, wherein the nucleic acid is DNA.
4. The method of claim 2, wherein the nucleic acid is RNA.
5. The method of claim 2, wherein said step (b) utilizes polynucleotide primers X and Y, wherein said primers X and Y anneal to nucleotides flanking the site of the mutation present in the *A2M-2* allele.
6. The method of claim 2, wherein said step (b) utilizes polynucleotide primers X and Y, wherein said primers X and Y anneal to nucleotides flanking the site of the mutation present in the *A2M-G* allele.
7. The method of claim 2, wherein said step (c) comprises sequencing the fragment to determine *A2M* genotype.
8. The method of claim 2, wherein said step (c) comprises RFLP analysis of the fragment to determine *A2M* genotype.

9. The method of claim 2, wherein said step (c) comprises size fractionation of the fragment to determine *A2M* genotype.

10. The method of claim 5, wherein said step (c) comprises sequencing the fragment to determine *A2M* genotype.

11. The method of claim 5, wherein said step (c) comprises RFLP analysis of the fragment to determine *A2M* genotype.

12. The method of claim 5, wherein said step (c) comprises SSCP analysis of the fragment to determine *A2M* genotype.

13. The method of claim 6, wherein said step (c) comprises sequencing the fragment to determine *A2M* genotype.

14. The method of claim 6, wherein said step (c) comprises RFLP analysis of the fragment to determine *A2M* genotype.

15. The method of claim 6, wherein said step (c) comprises SSCP analysis of the fragment to determine *A2M* genotype.

16. The method of claim 1, wherein said genotyping step comprises the steps of:

- (a) isolating DNA from an individual
- (b) subjecting said DNA to RFLP analysis thereby correlating *A2M* genotype with the occurrence of Alzheimer's disease.

17. The method of claim 16, wherein said RFLP analysis utilizes a restriction endonuclease specific for a restriction site created or deleted due to the pentanucleotide deletion found in *A2M-2*.

18. The method of claim 16, wherein said RFLP analysis utilizes a restriction endonuclease specific for a restriction site created or deleted due to the substitution mutation found in *A2M-G*.

19. A method for diagnosing Alzheimer's disease comprising: isotyping the Alpha-2-Macroglobulin protein of an individual.

20. The method of claim 19 comprising the steps of:

- (a) isolating protein from said individual
- (b) analyzing the protein thereby correlating Alpha-2-Macroglobulin isotype with the occurrence of Alzheimer's disease.

21. The method of claim 20, wherein said step (b) comprises western blot analysis of the protein to determine *A2M* genotype.

22. The method of claim 20, wherein said step (b) comprises ELISA analysis of the protein to determine *A2M* genotype.

23. The method of claim 20, wherein said step (b) comprises α_2 M electrophoretic mobility assay analysis of the protein to determine *A2M* genotype.

24. The method of claim 21, wherein said western blot analysis utilizes an antibody specific for the α_2 M-2 variant.

25. The method of claim 21, wherein said western blot analysis utilizes an antibody specific for the α_2 M Val¹⁰⁰⁰ variant.

26. The method of claim 22, wherein said ELISA analysis utilizes an antibody specific for the α_2 M-2 variant.

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27. The method of claim 22 wherein said ELISA analysis utilizes an antibody specific for the α_2 M Val¹⁰⁰⁰ variant.

28. A diagnostic kit for diagnosing Alzheimer's disease according to the method of claim 2, comprising: (i) a carrier means compartmentalized in close confinement therein to receive one or more container means; (ii) a container means containing polynucleotide primers X and Y, wherein said primers X and Y anneal to nucleotides flanking the site of the mutation present in the *A2M-2* allele; (iii) a container means containing α_2 M-1 DNA, or fragment thereof; and (iv) a container means containing α_2 M-2 DNA, or a fragment thereof.

29. A diagnostic kit for diagnosing Alzheimer's disease according to the method of claim 2, comprising: (i) a carrier means compartmentalized in close confinement therein to receive one or more container means; (ii) a container means containing the polynucleotide primers X and Y, wherein said primers X and Y anneal to nucleotides flanking the site of the mutation present in the *A2M-G* allele; (iii) a container means containing α_2 M Ile¹⁰⁰⁰ DNA, or fragment thereof; and (iv) a container means containing α_2 M Val¹⁰⁰⁰ mutant DNA, or a fragment thereof.

30. A diagnostic kit for diagnosing Alzheimer's disease according to the method of claim 20, comprising: (i) a carrier means compartmentalized in close confinement therein to receive one or more container means ; (ii) a container means containing an antibody specific for the α_2 M-2 variant; (iii) a container means containing an antibody specific for α_2 M-1; (iv) a container means containing the α_2 M-2 variant, or fragment thereof; and (v) a container means containing α_2 M-1, or fragment thereof.

31. A diagnostic kit for diagnosing Alzheimer's disease according to the method of claim 20, comprising: (i) a carrier means compartmentalized in close confinement therein to receive one or more container means; (ii) a container

means containing an antibody specific for the α_2 M Val¹⁰⁰⁰ variant; (iii) a container means containing an antibody specific for the α_2 M Ile¹⁰⁰⁰ protein; (iv) a container means containing the α_2 M Val¹⁰⁰⁰ variant, or fragment thereof; and (v) a container means containing the α_2 M Ile¹⁰⁰⁰ protein, or fragment thereof.

32. A diagnostic kit for diagnosing Alzheimer's disease according to the method of claim 23, comprising: (i) a carrier means compartmentalized in close confinement therein to receive one or more container means; (ii) a container means containing a protease; (iii) a container means containing a substantially purified sample of the α_2 M-2 variant; and (iv) a container means containing a substantially purified sample of the fast form of α_2 M-1.

For reference